

## **REMARKS**

### **1. Status of the Claims**

Claims 3-8 and 12-22 are pending. Claims 6, 7, 8, 12, 15, 16, 20, and 21 are herein cancelled. Claims 3, 4, 13, 14, and 18 have been amended.

Claims 3, 4, 14, and 18 have been amended to recite the 75% ester of hyaluronic acid. Claim 13 has been amended to change the dependency to claim 3.

No new matter has been added by way of these amendments.

### **2. Rejection Under 35 U.S.C. § 103**

The Examiner rejects claims 3-8 and 12-22 under 35 U.S.C. § 103 as being unpatentable over Davidson and Della Valle (USP 5,858,331) or alternately Davidson and Della Valle (EP341745).

#### **a. Zanellato Declaration 3 demonstrates that the present invention shows unexpected results.**

The Examiner states that Applicants “have not compared the closest prior art versus the claimed invention.” Applicants respectfully disagree that either of the Della Valle references is the closest prior art to the present application. Both references are listed second, and neither reference addresses wound healing or treatment for scarring.

However, to further rebut the Examiner’s incorrect positions, Applicants herein submit a third Declaration from Dr. Zanellato (hereinafter Zanellato Declaration 3), which compares the presently claimed invention to the embodiments disclosed in Della Valle (US 5,658,331) in a wound healing model. Specifically, the Zanellato Declaration 3 compares a 75% benzyl ester of Hyaluronic Acid as a non-woven fabric according to the present invention to a 100% benzyl ester of Hyaluronic acid in a perforated membrane as disclosed in Della Valle in claim 1, claim 12, and Examples 1-3. Zanellato Declaration 3 shows that the scarred areas of the claimed

invention were approximately 40% smaller than those of the total benzyl ester treatment at days 14 and 42.

Also, Dr. Zanellato describes that based on Della Valle, one of skill in the art would not apply a composition without cells seeded onto it because Della Valle applies a membrane of 100% esterified hyaluronic acid seeded with keratinocytes. (Zanellato Declaration 3, page 3). Thus, Dr. Zanellato concludes that for this additional reason, one of skill in the art would not find the present invention obvious.

Even further, the membrane and culture conditions of the Della Valle reference generate a two-dimensional cell growth, which ultimately leads to less proteoglycan generation. In contrast, the *in vivo* implantation of the present invention leads to a 3-dimensional cell growth with increased extracellular matrix (proteoglycans) and epithelial polarity and differentiation. (Zanellato Declaration 3, page 4). Applicants submit that one of skill in the art would not expect that modifying the membrane of Della Valle would obtain the benefits of an increase in proteoglycans and increased differentiation and polarization.

Applicants submit that these results would not have been expected to one of skill in the art based on the combination of Davidson and either of the Della Valle documents, and overcome any *prima facie* case of obviousness that may have been established. Accordingly, Applicants request that the rejections be withdrawn.

**b. The Examiner inappropriately dismisses the Declarations submitted with the Amendments of February 3, 2009 and March 9, 2009.**

The Examiner states on page 6 that the Zanellato Declarations 1 and 2 and the Abatangelo Declaration submitted with the Amendments of February 3, 2009 and March 9, 2009 are insufficient.

Specifically, the Examiner states that the Declarations are not sufficient because “[t]he increase in 40% wound healing is a matter of degree and not of unexpected result where the prior art as

discussed above specifically teaches of hyaluronic acid benzyl derivatives in treating scars and wounds.”

However, the Examiner’s position is not correct because the prior art does not specifically teach the use of hyaluronic acid benzyl derivatives in treating scars and wounds. While the Examiner’s proposed combination may arguendo teach the application of the benzyl derivatives for treating wounds, but no single reference suggests this combination, and Applicants here appropriately rebutted any *prima facie* case of obviousness with proper comparative tests.

Furthermore, the Examiner summarily dismisses the previously filed Declarations and simply states that “[t]he increase . . . is a matter of degree.” Applicants note that “[o]ffice personnel should not . . . summarily dismiss [evidence of secondary considerations] as not compelling or insufficient. If the evidence is deemed insufficient to rebut the *prima facie* case of obviousness, Office personnel should specifically set forth the facts and reasoning that justify” a conclusion that evidence of secondary considerations is insufficient to overcome a *prima facie* case of obviousness. MPEP § 2145.

Here, the Examiner has provided no reason why an increase in 40%-50% wound healing (i.e., a 40%-50% increase in the amount of wound re-epithelialization) would be expected, especially when a comparison of the claimed invention to embodiments from both Davidson (Declarations submitted with the Amendments of February 3, 2009 and March 9, 2009) and Della Valle (Zanellato Declaration 3, attached) shows an approximate 40%-50% increase in wound healing obtained with the claimed invention.

Lastly, the prior art embodiments only show at most, 5-8% improvement in the area of wound healing. (Compare Zanellato Declaration 2, Experiment 2, column D, and Zanellato Declaration 3, Graph, column B). Thus, *at the very least*, the present invention was approximately **7 times more effective** than the embodiments disclosed in the prior art. Thus, Applicants submit that the increased area of wound healing would NOT have been expected by one of skill in the art based on the combined disclosures of Davidson and Della Valle (USP 5,858,331 or EP341745).

Applicants submit that the unexpected results presented in the three Zanellato Declarations and the Abatangelo Declaration overcome any *prima facie* case of obviousness that the Examiner may have established. Accordingly, Applicants request that the obviousness rejections be withdrawn.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a three (3) month extension of time for filing a reply in connection with the present application, and the required fee of \$1,110.00 is attached hereto.

If the Examiner has any questions concerning this application, the Examiner is requested to contact Leonard R. Svensson, Reg. No. 30,330 at the telephone number of (858) 792-8855. Facsimile communications may be sent to Leonard R. Svensson at the facsimile number of (858) 792-3785.

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Respectfully submitted,

By  <sup>#58,303</sup>

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Attachment: Zanellato Declaration 3